Case Series: Four Cases of Anorexia Nervosa Concomitant with Central Adrenal Insufficiency

Sunao Matsubayashi (smpsmjp@yahoo.co.jp)
Fukuoka Tokushukai Hospital https://orcid.org/0000-0002-0896-2816

Madoka Tanaka
Department of Psychosomatic Medicine, Endocrinology and Diabetes Mellitus, Fukuoka Tokushukai Hospital

Takeshi Hara
Department of Psychosomatic Medicine, Endocrinology and Diabetes Mellitus, Fukuoka Tokushukai Hospital

Case report

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Abstract

Objective: Widespread attention has been paid to the misdiagnosis of life-threatening Addison's disease as anorexia nervosa. However, there are no reports on the possible comorbidity of Addison's disease and other adrenal insufficiencies with anorexia nervosa.

Methods: A case-series presentation of anorexia nervosa concomitant with central adrenal insufficiency.

Results: Four anorexia nervosa patients (21-35 years old, all females) complained of severe fatigue during their treatment. After a thorough examination of the hypothalamus-pituitary-adrenal axis using stimulation with a rapid adenocorticotropic hormone test of 250-μg Cortrosyn®, a corticotropin-releasing hormone test, and an insulin tolerance test, central adrenal insufficiency was diagnosed. Two of the four patients had a history of exogenous steroids for their history of comorbidity. One of the residual two patient had Rathke's cleft cyst. After the initiation of hydrocortisone replacement the patient's fatigue symptoms improved and they were able to return to school and their workplace. In some cases, their weight obsession was reduced after the initiation of hydrocortisone replacement.

Conclusion: Anorexia nervosa may be concomitant with central adrenal insufficiency partly in relation to exogenous steroids used for their history of comorbidity, which needs to be kept in mind when treating such patients.

Level of Evidence

Level V, descriptive study.

Introduction

The clinical symptoms of anorexia nervosa and Addison's disease are similar [1]. Addison's disease has been misdiagnosed as anorexia nervosa in some cases [1, 2]. In contrast to Addison's disease, however, the hypothalamius-pituitary-adrenal (HPA) axis is activated in anorexia nervosa [3].

We herein report four cases of anorexia nervosa concomitant with central adrenal insufficiency diagnosed by examining the HPA axis, as the patients complained of severe fatigue and excessive daytime sleepiness during weight loss.

Case Presentation

Case 1. 22-year-old female, a university student

At 14 years old, the patient had been troubled by her relationship with her classmates who ignored her, stopped going to school, and became withdrawn; as a result, her weight naturally increased. When she entered high school, she weighed 82 kg (height 163 cm) (body mass index [BMI] 30.9 kg/m^2) and was pointed out as obese at a school medical checkup. She learned from the Internet that self-induced

vomiting could help her lose more weight, so she began to binge-eating and vomit. As a means of vomiting, she used to put her hands in her mouth, but gradually used the handle of a spoon and pressed it against her pharynx to induce the vomiting reflex.

She was admitted to a psychiatric hospital and underwent cognitive-behavioral therapy, but her binge-eating and vomiting persisted, so she was referred to our outpatient psychosomatic medicine clinic at 16 years old. At her visit to our clinic, she complained of depression and daytime sleepiness in addition to bulimia and vomiting. Her weight was 44.5 kg (BMI 16.7 kg/m^2) at the time of her first visit. A previous medical doctor had prescribed nortriptyline 30 mg, sulpiride 150 mg, clotiazepam 15 mg, and brotizolam 0.25 mg. The patient's medical history included childhood asthma. Her parents are divorced and she lives with her mother, sister, and maternal grandmother. She had taken inhaled steroids until reaching junior high school age (Table 1).

No abnormalities were noted on her physical examination. The patient was diagnosed with anorexia nervosa (binge-eating/purging type) and depression (Table 1). She was prescribed fluvoxamine 75 mg and brotizolam 0.25 mg and treated with psychoeducation for anorexia nervosa and supportive therapy. At 19 years old, her weight had been restored to 53 kg (BMI 19.9 kg/m^2), but she repeatedly binge-eating when she felt stressed. Around 20 years old, she began to experience hives frequently and panic attacks. She also became very aware of fatigue and was still concerned about her weight.
At 21 years old, we diagnosed her with central adrenal insufficiency based on three cortisol stimuli tests including a rapid adrenocorticotropic hormone (ACTH) test using 250-μg Cortrosyn® (Dai-ichi Sankyo Pharmaceutical Co., Tokyo, Japan), a corticotropin-releasing hormone (CRH) test using 100 μg human corticorelin (hCRH "Tanabe" injection 100 μg; Nipro ES Pharma, Osaka, Japan), and an insulin tolerance test (ITT) using 0.1 U/kg regular insulin (Novolin R®; Novo Nordisk A/R, Tokyo, Japan); ≥ 496.6 nmol/L of peak cortisol levels in response to the CRH test or the ITT, and cortisol levels at 30 minutes after the rapid ACTH test was judged to be a normal response according to adrenal insufficiency practical guideline [4] (Table 2).

Pituitary magnetic resonance image (MRI) did not show any significance. She was administered 10–15 mg of hydrocortisone, and her physical condition recovered. At 22 years old, she said that she felt more human and began to express herself as she used to. Her binge-eating episodes became less frequent after the initiation of hydrocortisone.

Case 2. 36-year-old female, an office worker

As a university student, she became obsessed with her weight and shape and gone on a diet. Her weight decreased from 41 kg (height 154 cm) (BMI 17.3 kg/m^2) to 35 kg (BMI 14.8 kg/m^2), and she felt proud of herself for achieving thin physique. At 25 years old, she visited a university hospital and was diagnosed with anorexia nervosa, and was treated with mindfulness-based stress reduction. At 29 years old, she weighed 37.5 kg (BMI 15.8 kg/m^2) at the time of her visit to our department and had a Beck depression inventory (BDI) score of 45 (reference range ≤ 15). Her psychosocial background was that her parents had fought constantly since she could remember, and they divorced when she was 9 years old. In order to

avoid excessive parental interference, she devoted herself to her studies and excelled in high school. However, she was unable to maintain stable interpersonal relationships, and did overdose on drugs and cut her wrists at 27–28 years old several times for suicide attempt. However, she has managed to adapt to society as a company employee.

She complained of strong menstrual pains, a lack of energy, and fatigue. She had no self-acceptance and often wished she had never been born. She was diagnosed with anorexia nervosa and depression and prescribed escitalopram 10mg (Table 1). There was no obvious exogenous steroid-using history. Although her weight did not fluctuate significantly, she was obsessed with her weight, had persistent fatigue, irritability, and emotional incontinence, and began to take long absences from work due to insomnia and excessive daytime sleepiness. A diagnosis of central adrenal insufficiency was made by cortisol stimulation tests (Table 2). Pituitary MRI revealed Rathke's cleft cyst. After administration of 15 mg of hydrocortisone, her fatigue improved and she was able to return to her workplace. No obvious weight gain was noted after the administration of hydrocortisone, and her weight persisted.

Case 3. 22-years-old female, a university student

At 19 years old, when she was attending a preparatory school for university entrance exams, she became unable to eat, and her weight of 43 kg (height 159 cm) (BMI 17.0 kg/m^2) gradually decreased to 41 kg (BMI 16.2 kg/m^2), which led to amenorrhea; at 20 years old, her weight dropped to 31 kg (BMI 12.2 kg/m^2). She was referred to our department for consultation.

She weighed 27.7 kg (BMI 10.9 kg/m^2) at the time of her first visit. Her medical history was unremarkable. She had never expressed her desire to be thin, but there was no effort to gain weight. She still remembers the stress of examinations, the over-interference of her mother who was a teacher, and the problems she had in her relationships with people in the high school brass band.

At the time of her first visit, there was no obvious abnormalities in her physical appearance other than emaciation, and she was not overactive. She has no history of exogenous steroid use. She was diagnosed with anorexia nervosa (Table 1).

After being hospitalized for two months to improve her nutrition, her weight recovered to 33 kg (BMI 13.1 kg/m^2). She was diagnosed as adrenal insufficiency based on an HPA axis test (Table 2) and was treated with 10 mg of hydrocortisone. She was able to return to school but did not gain any weight, and his weight has remained at 33–34 kg (BMI 13.1–13.4 kg/m^2).

Case 4. 31-year-old female, an office worker

A 31-year-old woman, an office worker, was referred to our clinic by her physician. She complained of weight loss of 8kg and a depressed mood. She had been suffering from allergic dermatitis between elementary and junior high school and often used topical steroids. Six months before she visited our clinic she received an invitation to a wedding ceremony from a friend. Since that time, she started the diet to wear a fitting dress. On the other hand, she did not have any desire to gain weight and was satisfied

with her weight loss. However, she quit work because of tired. Her weight at the time of the first examination was 40 kg (height 163 cm) (BMI 15.1kg/m^2), blood pressure 90/62 mmHg, and pulse rate 60/min. No obvious abnormalities on physical examination except for thinness, her BDI was 22. The patient was diagnosed with anorexia nervosa, a restrictive type associated with depression. Psychoeducation was provided to convey the importance of eating and encourage food intake step by step. On the other hand, if she did not gain weight or recover from her symptoms, she should be transferred to the inpatient ward. Escitalopram 10mg was prescribed. Three months after her first visit, her weight had gradually recovered to 43 kg (BMI 16.2 kg/m^2), but she did not wish to gain anymore. Around this time, she complained of uncomfortable feelings after eating. She also felt fatigued (Table 1).

Considering the possibility of reactive hypoglycemia, a 4-hour 75g-oral glucose tolerance test was performed, and the unpleasant symptoms were reproduced at 180 minutes of glucose loading. The blood glucose level at that time was 2.6 mmol/L (5.0 mmol/L before glucose loading). The HPA axis was also examined, and central adrenal insufficiency was diagnosed (Table 2). Pituitary MRI did not show any abnormality. To prevent reactive hypoglycemia, a divided diet was recommended to her and a prescription of 5mg of hydrocortisone was taken only once when she felt fatigued in addition to escitalopram. At 2 years since the initial visit to our clinic, her body weight recovered to 47 kg (BMI 17.7 kg/m^2). She started another work.

Discussion

Although anorexia nervosa has been said to be characterized by thinness and hyperactivity [5], according to the DSM-5 diagnosis [6], it is generally characterized by a restriction of energy intake and fear of going weight or becoming fat and the way in body weight or shape is prescribed. Hyperactivity was not necessarily being a diagnostic criterion.

The four cases of anorexia nervosa presented in this case-series were characterized by the impaired perception of weight and body shape, but no obvious hyperactivity, and symptoms such as fatigue or excessive sleepiness in addition to an obsession with weight and shape were reported. Fatigue is also seen in anorexia nervosa, but the core symptoms of anorexia nervosa are thinness and hyperactivity [5], which are slightly different from the clinical symptoms of anorexia nervosa that we often encounter.

In the present cases, we examined the HPA axis to exclude adrenal insufficiency, given the persistent fatigue reported. Two patients (except two) showed cortisol levels of less than 496.6 nmol/L at 30 minutes after loading in the rapid ACTH test, and three patients (except one) showed peak cortisol levels of less than 496.6 nmol/L in response to the CRH. The peak cortisol levels of the three patients who underwent ITT were all < 496.6 nmol/L. Basal ACTH levels were lower than reference range or low in the reference range in these present patients. The diagnosis of central adrenal insufficiency was therefore made.

Pituitary imaging showed Rathke's cleft cyst in one patient. Exogenous steroid use was found in two of the four patients. The etiology of central adrenal insufficiency varies widely, but the use of exogenous steroid hormones, such as inhaled steroids, is thought to be the most common cause [7]. After the diagnosis of central adrenal insufficiency, 5–15 mg of hydrocortisone replacement improved the quality of life of these four patients by relieving their symptoms of fatigue and daytime sleepiness, and they were able to return to school and their workplace after receiving hydrocortisone. Furthermore, in three of the four patients diagnosed with anorexia nervosa, no weight gain was evident after the initiation of hydrocortisone, but binge-eating episodes were reduced, suggesting that central adrenal insufficiency had been involved in some of the symptoms of their anorexia nervosa.

Although Addison's disease has been cited as the most common differential diagnosis for anorexia nervosa, it is important to note that central adrenal insufficiency may also be comorbid with anorexia nervosa.

Conclusion

HPA axis tests showed central adrenal insufficiency in four patients with anorexia nervosa partly in relation to past exogenous steroids used or Rathke's cleft cyst. Replacement of hydrocortisone improved their social conditions, and they were able to return to school and their workplace with reduced binge-eating episodes, although the bodyweight was not fully restored.

Abbreviations

ACTH, adrenocorticotropic hormone; BDI, Beck depression inventory; BMI, body mass index; CRH, corticotropin-releasing hormone; HPA, hypothalamus-pituitary-adrenal; ITT, insulin tolerance test; MRI, magnetic resonance image

Declarations

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None.

Authors’ contributions

Sunao Matsubayashi was a physician and contributed to the writing and editing of the manuscript. Madoka Tanaka and Takeshi Hara were involved in the editing of the manuscript

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Availability of data and materials

This report is a case series. The important data have been described in the text. Due to privacy and ethical concerns, neither further data nor the source of the data can be made available.

Ethics approval and consent to participate

The present study was performed in accordance with the Declaration of Helsinki as amended in 2008. The present study was approved by the Ethics Committee of Fukuoka Tokushukai Hospital (Approval No. O-2101).

Consent for publication

All participants provided their written informed consent.

Conflict of Interest

The authors declare no conflicts of interest in association with the present study.

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Tables

Due to technical limitations, table 1,2 is only available as a download in the Supplemental Files section.

Supplementary Files

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- Table1.jpg
- CareChecklist.docx
- Table2.jpg